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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,675	12/17/2004	Mohammad R. Marzabadi	67442-A-PCT-US	6779

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EXAMINER	
O'DELL, DAVID K	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
03/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,675	MARZABADI ET AL.	
	Examiner	Art Unit	
	David K. O'Dell	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-14,17,18 and 22-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-14,17,18 and 22-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *29 January 2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 3-14, 17, 18, 22-28 are pending in the current application.

This application is a 371 of PCT/US03/21391 filed 07/03/2003, which is a CON of 10/189,145 filed 07/03/2002 (now abandoned).

Response to Arguments

2. Applicant's arguments filed on January 29, 2008 have been fully considered but they are not fully persuasive. The objections to the claims for non-standard abbreviations are withdrawn in light of the amendments canceling the claims. The rejections of the claims under 35 U.S.C. 102 (a), and 102(e) over Salon et. al. are maintained, although for different reasons now since the applicant has amended the claims around the rejection. The 112 1st paragraph rejection is maintained, because R_3 has not been limited to phenyl. This rejection is NON-FINAL, since claim 4 is now rejected under new grounds.

Under examination:

I. Claims 1-14, 17, 18, 22-26, 27, 28 drawn to compounds, compositions and processes of making said compositions having a piperidinyl-benzamide-phenyl core as depicted in the structures of claim 4 and claim 22 only. If this group is elected, an election of a single disclosed species of compound is required. Further restriction will be made based on the election.

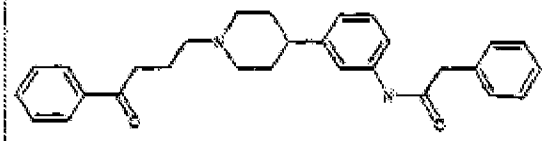
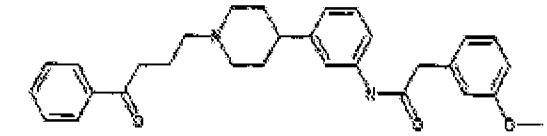
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

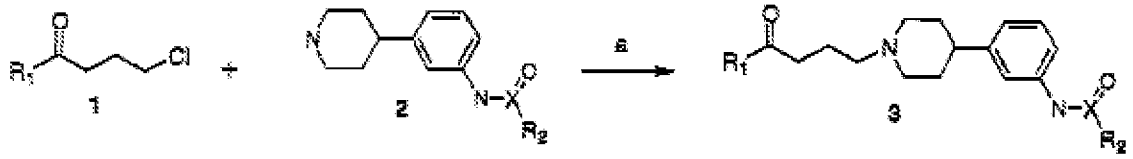
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 3, 4, are rejected under 35 U.S.C. 102(a) as being inherently anticipated by Salon, et. al. WO 2002002744 A2. Salon teaches the following compounds: Where each A is H, Z is carbonyl, n is 1, and R_4 is phenyl, R_2 is alkyl a compound of the instant claims is produced. Salon discloses several compounds (compounds 60, 61, 68, 75, 76, 79, 80, 83) which have the same piperidinyl-benzamide moiety of the instant case as shown below:

75		508
76		21

These compounds were reportedly prepared by the alkylation of the piperidines (2) with butrylcholrides (1) as a shown below:

Scheme E: General Synthesis of the MCH Antagonists



While the unsubstituted piperidines are not named expicitly in each case, they are required for the preparation of the compounds 60,61,68,75,76, 79, 80 & 73 as evidenced by the procedures below:

General procedure for the Preparation of the substituted 4-N-(3-(1-[4-(phenyl)-4-oxobutyl]-4-piperidinyl]phenyl)acetamides:

A mixture of N-[3-(4-piperidinyl)phenyl]acetamide (1.0 eq) and an aryl substituted chlorobutyrophenone (2.0 eq), K_2CO_3 (5.0 eq), diisopropylethylamine (3.0 eq) and tetrabutylammonium iodide (cat. 5-10%) in dioxane (0.5 to 1.0 M) were heated at reflux temperature for 16 h. The reaction mixture was filtered and concentrated *in vacuo*. The crude product was chromatographed using silica preparative TLC (chloroform : methanol containing 0.5% isopropyl amine) to give the desired product.

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Example 58

N-{3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of 0.0500 g (0.200 mmol) of 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide, 0.100 g (0.400 mmol) of 4-chloro-3',4'-dimethylbutyrophenone, 0.080 g (0.600 mmol) of K_2CO_3 and 0.090 g (0.600 mmol) of NaI in 5 mL of DMF was heated at reflux temperature for 18 hours. The reaction mixture was filtered, the filtrate was poured into 5 mL of water and washed with 3 X 5 mL of ethyl acetate. The combined organic extracts were dried ($MgSO_4$), concentrated in vacuo and purified by preparative TLC (silica; 9.5 : 0.5, dichloromethane : methanol + 1% isopropyl amine) to afford 0.067 g (80.0% yield) of the desired product: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, 1H, J=8.0 Hz), 7.44 (s, 1H), 7.38 (d, 1H, J=8.0 Hz), 7.23-7.20 (m, 2H), 7.16 (s, 1H), 6.95 (d, 1H, J=6.8 Hz), 3.13-3.11 (m, 2H), 3.02 (t, 2H, J=7.0 Hz), 2.56-2.40 (m, 4H), 2.32 (s, 6H), 2.17-2.15 (m, 2H), 2.04-1.78 (m, 6H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e : 421.3 (M + H)$^+$.

These compounds are in fact inherently disclosed, since the piperidines of the instant case are used in the process of Salon et. al.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 3, 4, are rejected under 35 U.S.C. 102(e) as being inherently anticipated by Salon, et. al. WO 2002002744 A2. *Vide supra* for discussion.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 3, 17, 18, 26, 27, & 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain compounds it does not reasonably provide enablement for the scope of compounds bearing the extensive list of substituents. The compounds that are enabled are as follows:

R3 should be limited to phenyl (in the definition of R4).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to the following:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention
In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(A) The breadth of the claims: The claims are very broad encompassing all heteroaryls, aryls and other groups bearing multiple substitutions **(B) The nature of the invention:** This is a chemical invention requiring the synthesis of compounds and such compounds should have activity at MCH receptor. **(D) The level of one of ordinary skill**: One of ordinary skill is a practicing organic/medicinal chemist. **(C) The state of the prior art: (E) The level of predictability in the art: (F) The amount of direction provided by the inventor, (G) The existence of working examples, and (H) The quantity of experimentation needed to make or use the invention:** Each one of the factors (**C**, **E-H**) will be discussed in light of the scientific literature when such a factor is being directly pointed to a large capital letter referring to the aforementioned Wands factor will be placed directly after such a remark or explication.

The limitations of activity at MCH are well known. What are the important structural features for the claimed utility? It is clear from the data in the specification that the structural features of the compound are of paramount importance for activity. All the compounds have R as H, and more tellingly have a very precise halo susbstitution pattern with A as fluoro. **(H)** The medicinal chemistry of MCH is relatively well-developed and many limitations are well known in the art. **(C)** It is sensitive to structural changes that may be relatively minor in the chemical sense see some analogous compounds of Guo et. al. "Discovery and SAR of biaryl piperidine MCH1 receptor antagonists through solid-phase encoded combinatorial synthesis" *Bioorganic & Medicinal Chemistry Letters* **2005**, *15*, 3696–3700, whole document. **(F)** In particular see the discussion on pg. 3698 paragraph 2, in reference to the substitution of the phenyl group with heteroaryls:

> "Replacement of the 3-pyridyl group at R1 with either an alkyl group, such as methyl (8g), or a fused heterobicycle, **such as 5-indolyl (8h), caused potency decreases of 100-fold or more**, relative to 8e. However, replacing the 3-pyridyl at R1 with 3-substituted phenyl groups, such as 3-Cl-, AcHN-, OHC-, or NC-phenyl gave compounds with potency (8i–l, Ki = 1.4–5.5 nM) similar to that of 8e."

No such compounds bearing heteroaryl groups have been prepared. We have been given little information in regard to the molecular determinants of receptor affinity for the compounds of the instant case. **(F & G)** In this case these compounds bear a remarkable structural resemblance to one another, yet the claims are not commensurate in scope. The factors outlined in *In Re Wands* mentioned above apply here, and in particular As per the MPEP 2164.01 (a): "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." It is very clear that one could not make/use this very broad invention that has only four working examples in this unpredictable art without undue experimentation. **(C, E, F, G, H).**

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 3-14, 17, 18, 22-28 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 of copending Application No. 11/034,611. Although the conflicting claims are not identical, they are not patentably distinct from each other because they cover the same compounds.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David K. O'Dell whose telephone number is (571)272-9071. The examiner can normally be reached on Mon-Fri 7:30 A.M.-5:00 P.M EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Primary examiner, Rita Desai can be reached on (571)272-0684. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

D.K.O.